

Trend Watch



Antipsychotic Use Varies by Patient Age

by Elisa F. Cascade and Amir H. Kalali, MD

Featuring expert commentary from
Leslie Citrome, MD, MPH

ABSTRACT: Since their introduction in mid 1990's, atypical antipsychotics have been studied in a ever-expanding number of conditions. To gain a better understanding of current practice patterns, we investigated antipsychotic uses across different patient age groups. In both the 18 to 39 and 40 to 64 age groups, schizophrenia (ICD-9 295) and affective psychoses (ICD-9 296) account for approximately 70 percent of atypical antipsychotic use. In contrast, these diagnoses only represent 41 percent of use in patients age 0 to 17 and 36 percent in patients age 65 and older.

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INTRODUCTION

Since their introduction in mid 1990s, atypical antipsychotics have been studied in a ever-expanding number of conditions. To gain a better understanding of current practice patterns, we investigated antipsychotic uses across different patient age groups.

METHODS

We obtained data from the following two sources: 1) total retail prescriptions of antipsychotics by age from Vector One National (VONA), which captures nearly half of all prescription activity in the US and 2) annual data from Verispan's Prescription Drug and Diagnosis Audit (PDDA) database regarding most common uses of antipsychotics by age. PDDA is a syndicated data product

that captures information from a rotating panel of 3,100 office-based physicians representing 29 specialties across the United States. Each panel member completes a one-page log on demographics, diagnoses, and medications for every patient seen during the reporting period.

RESULTS

Forty-five percent of atypical antipsychotics are prescribed to patients age 40 to 64. As seen in Figure 1, an additional 24 percent of antipsychotics are used by patients aged 18 to 39. The two remaining patient age groups, under 18 and ≥ 65 , accounted for 14 percent and 17 percent of antipsychotic use respectively.

Figure 2 displays the most common uses of atypical antipsychotics by age; diagnoses accounting for at least five percent of total use are pictured. In both the 18 to 39 and 40 to 64 age groups, schizophrenia (ICD-9 295) and affective psychoses (ICD-9 296) account for approximately 70 percent of atypical antipsychotic use. In contrast, these diagnoses only represent 41 percent of use in patients age 0 to 17 and 36 percent in patients age ≥ 65 .

For patients age 0 to 17, in addition to schizophrenia and affective psychoses, hyperkinetic syndrome (ICD-9 314) was also a common reason for antipsychotic use, accounting for 16 percent of diagnoses. Dementia was the other most common reason for atypical antipsychotic use in patients age ≥ 65 , with 17 percent of diagnoses.

EXPERT COMMENTARY

by Leslie Citrome, MD, MPH

Off-label use of antipsychotic medications for patients is controversial because of the limited

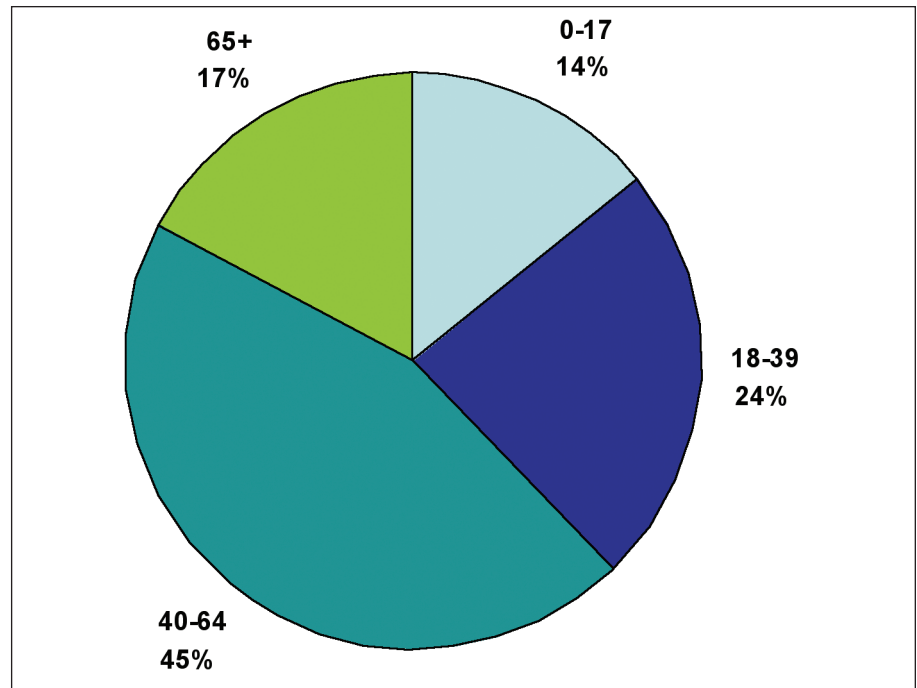


FIGURE 1. Atypical antipsychotic use by patient age.

Source: Verispan VONA, TRx USC 64190 Atypical Antipsychotics, 2006.

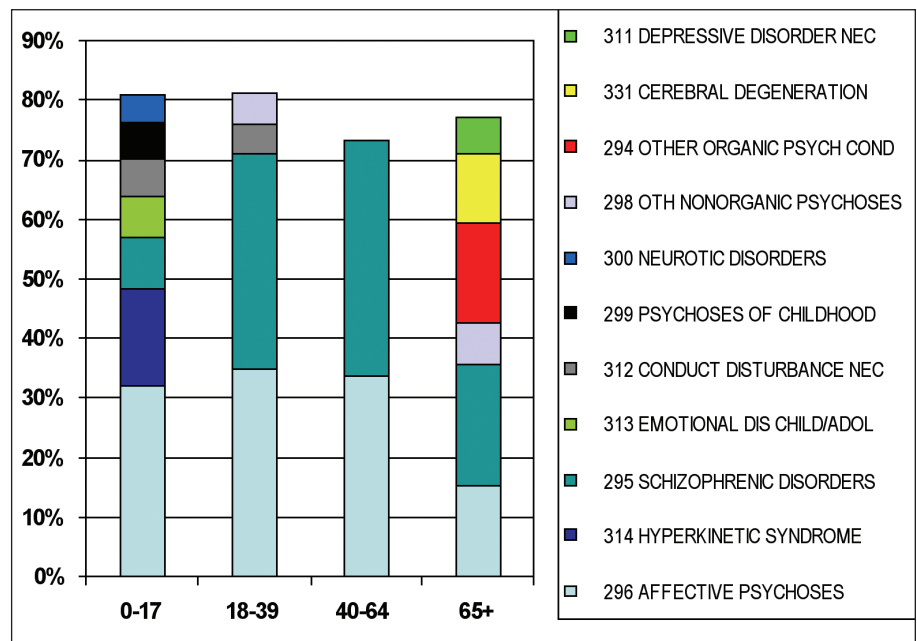


FIGURE 2. Most common uses of atypical antipsychotics by age.

Source: Verispan PDDA 3-Digit Dx for Atypical Antipsychotics, 2006. Diagnoses accounting for at least 5% of antipsychotic uses are included.

TABLE 1. Age distribution of the US Population and of atypical antipsychotic medication prescriptions

Age group	Percentage of Prescriptions	Percentage in Population
Less than 18 years	14%	26%
18–64 years	69%	61%
65 years or older	17%	12%

evidence base supporting the efficacy of this as well as the potential for adverse events.¹ Children and the elderly are two at-risk populations for which antipsychotic medications can be both helpful and potentially problematic. Cascade and Kalali observed that 14 percent and 17 percent of prescriptions of atypical antipsychotic medications were accounted for by patients in the age groups of less than 18 years and 65 years and older, respectively. Moreover, nonpsychotic disorders represented 59 percent of use in patients less than 18 years of age and 64 percent in patients age 65 years and older.

Pharmaceutical companies are restricted from marketing off-label uses of their products, including the pediatric use of agents only approved for adult use, as well as off-label diagnoses. Nevertheless, the agents are used extensively and the potential market is substantial. Table 1 provides the age distribution for the general US population as determined from census data² together with Cascade and Kalali's data on distribution of prescriptions of atypical antipsychotic medications.

A concern has been expressed about the exposure of persons under the age of 18 years to antipsychotic medications in the face of the lack of

controlled clinical trials supporting this practice.^{3,4} Of particular alarm are endocrine and metabolic adverse effects of atypical antipsychotics.⁵ As per the data presented by Cascade and Kalali and the demographic distribution of the US population, the age group less than 18 years is not overrepresented in terms of numbers of prescriptions of atypical antipsychotics. Nonetheless, Aparasu and Bhatara³ found that among patients younger than 20 years examined using the 2003 to 2004 National Ambulatory Medical Care Survey and the outpatient department portion of the 2003 to 2004 National Hospital Ambulatory Medical Care Survey, that antipsychotic medications were prescribed in two million outpatient visits annually, representing one percent of overall visits by children and adolescents in 2003 to 2004. Most (99%) of these visits involved prescribing of atypical agents, more frequently risperidone, quetiapine, and aripiprazole, and more often in patients over nine years, males, and whites. Diagnoses associated with antipsychotic prescribing were bipolar disorder, psychoses, depression, disruptive behavior, and anxiety. Similar findings were reported by Olfson and colleagues,⁶ where national trends and patterns in antipsychotic treatment of

youth seen by physicians in office-based medical practice were examined for the period 1993 to 2002. As with Aparasu and Bhatara,³ patient visits by persons 20 years and younger from the National Ambulatory Medical Care Surveys were studied. The estimated number of office-based visits by youth that included antipsychotic treatment increased from approximately 201,000 in 1993 to 1,224,000 in 2002. Overall, 9.2 percent of mental health visits and 18.3 percent of visits to psychiatrists included antipsychotic treatment. From 2000 to 2002, 92.3 percent of visits with prescription of an antipsychotic included an atypical agent. Diagnoses recorded included disruptive behavior disorders (37.8%), mood disorders (31.8%), pervasive developmental disorders or mental retardation (17.3%), and psychotic disorders (14.2%).

There are additional concerns about the prescription of antipsychotics to persons 65 years or older, particularly among those with dementia. Cascade and Kalali found that among the patients 65 years and older receiving atypical antipsychotics, dementia was a commonly stated indication. Atypical antipsychotics, such as olanzapine and risperidone, can successfully reduce aggression and/or psychosis in patients with dementia,⁶ however the US Food and Drug Administration issued a Public Health Advisory in 2005 regarding deaths with antipsychotics in elderly patients with behavioral disturbances,⁷ and consequently, the manufacturers of all of the atypical antipsychotics were required to include a boxed warning regarding this risk. Gill and colleagues⁸ recently reported a population-based retrospective cohort study of antipsychotic use and all-cause mortality in older adults with dementia residing in Ontario, Canada, and found that the new use of atypical antipsychotics (approximately 75% were using risperidone, 20%

olanzapine, and 5% quetiapine) was associated with a statistically significant increase in the risk for death at 30 days compared with non-use. Typical antipsychotic use (approximately 60% were using haloperidol, 18% loxapine, 10% thioridazine, 6% chlorpromazine, and 4% perphenazine) was associated with higher risk of mortality than for atypical antipsychotics. The data presented by Gill and associates⁸ is

[According to Olfson, et al.,]⁴ the estimated number of office-based visits by youth that included antipsychotic treatment increased from approximately 201,000 in 1993 to 1,224,000 in 2002...Diagnoses recorded included disruptive behavior disorders (37.8%), mood disorders (31.8%), pervasive developmental disorders or mental retardation (17.3%), and psychotic disorders (14.2%).

consistent with a meta-analysis⁹ of prospective double-blind placebo-controlled trials where risk of death was 54-percent higher among the atypical antipsychotic group versus the placebo group. However, mortality risk appears higher with the older antipsychotic agents, and this disadvantage for the older agents was also observed in two other population-based studies,^{10,11} where short-term mortality in elderly people who were prescribed typical antipsychotics was approximately 50-percent higher than those prescribed atypical agents. Thus, risk of intervening with an antipsychotic requires a careful risk benefit evaluation. Certain populations will benefit from this intervention as noted in a small number of very frail patients with dementia, mean age 86 years, in a prospective Finnish study.¹² They found that about half of the patients used antipsychotic medication and that mortality within two years was 32 percent for those who received an atypical antipsychotic, 45 percent for those who received a typical

antipsychotic, and 50 percent for those who did not use antipsychotics.

In summary, Cascade and Kalali provide some sobering statistics of potentially problematic off-label use of atypical antipsychotics in two vulnerable populations. The current use of these agents in children, adolescents, and the elderly should be carefully thought through in terms of potential risks versus benefits. Additional research in the form of

controlled clinical trials involving children, adolescents, and the elderly should be undertaken for indications that show substantial promise.

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